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          and Diet in African American and Caucasian Men

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13. ABSTRACT (Maximum 200 Words)

The study aims to determine racial differences between insulin-like growth factor-1 (IGF-1), insulin-like binding protein-1 (IGFBP-2), insulin-like binding preotein-3 (IGFBP-3), prostate specific antigen (PSA), testosterone, body mass index (BMI), and diets high in calories, protein and fat. Specifically, the primary objectives are to:

- define racial differences in serum levels of free and total IGF-1, IGFBP-2, IGFBP-3, and testosterone
- define how diet and BMI impact serum levels of IGF-1, IGFBP-2, IGFBP-3, testosterone and PSA in African American and Caucasian men.
- determine the associations between serum levels of free and total IGF-1, IGFBP-2, IGFBP-3, testosterone, PSA, BMI and specific nutrients.

Over 500 African American and Caucasian men were recruited. There were no racial differences found for serum levels of IGF-1. These analyses show that IGFBP-2 is significantly lower in African American than white men, while IGFBP-3 and testosterone are significantly higher. IGFBP-2 also exhibits a significant inverse association with BMI for both races, and a positive association with age for whites. African American men have higher consumption of calories, protein, total fat and nutrients than whites; all but the latter differences are significant. Finally, IGFBP-2 exhibits a significant univariate negative correlation with calories, protein and total fat, with a somewhat stronger association among white than African American men. Adjustment for age and BMI made all but the association with calories no longer significant, but it is possible that this represents over-adjustment of the model since age I not significantly correlated with nutrient intake in these men.

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INTRODUCTION

Presently, prostate cancer is the most common cancer in U.S. males. In 1999, the American Cancer Society estimates that 179,300 new cases will be diagnosed and approximately 37,000 men will die from metastatic prostate cancer (1). The incidence and mortality rates are even greater in African-American men than among other racial or ethnic populations in the world. Prostate cancer incidence rates are nearly two times higher for African-American men than for white men (2). The incidence and mortality rate for prostate cancer in the Washington, D.C. area is the highest in the world. Moreover, the rate of increase in prostate cancer occurs earlier for black males than white males (3). Evidence suggest that African Americans may be at higher risk since they consume diets higher in energy and fat and have made smaller changes in decreasing fat intake when compared to Caucasian men (4).

Insulin-like growth factor-1 (IGF-1) and IGF-binding proteins have been implicated in the carcinogenesis of breast, prostate and other hormone dependent cancers. Insulin-like growth factor-1 functions in an autocrine and paracrine manner to promote normal growth and malignant cellular proliferation (5-7). IGF-1 is produced by normal prostate cells (8) prostate cancer cells (9) and has mitogenic and antiapoptotic effects (10,11) on prostate epithelial cells (12). Several epidemiological studies have shown increased plasma levels of IGF-1 to be a strong risk factor for prostate cancer (13-15). Chan et al. (14) examined plasma levels of IGF-1 and IGFBP-3 in a prospective case-control study and found mean levels of IGF-1 to be significantly elevated among the prostate cases when compared to the controls. The relative risk was 4.3 (95% CI= 1.8-10.6) for men in the highest quartile of IGF-1 levels when compared with men in the lowest quartile. Higher plasma IGF-1 concentrations were associated with higher rates of malignancy in the prostate gland. Also, plasma levels of IGFBP-3 were inversely associated with risk after controlling for IGF-1 levels.

Another study (15) found a statistically significant positive association between serum levels of IGF-1 and risk of prostate cancer (OR=1.51; 95% CI=1.0-2.26 per 100 ng/ml increment). In this study serum levels of IGFBP-3 were not significantly associated with prostate cancer risk. However, Kanety et al. (16) found that patients with metastatic prostate cancer had significant reductions in both the absolute and relative amounts of IGFBP-3 and significantly higher serum IGFBP-2 concentrations when compared with the controls. The authors suggested that IGFBP's might be involved in growth modulation of prostate malignancy.

Several researchers have reported elevated serum IGFBP-2 concentrations (16-18) in patients with prostate cancer. It was suggested that elevations in serum IGFBP-2 concentrations might be unique to the carcinomatous condition (17). Ho et al. (18) suggested that IGFBP-2 might function as an IGF scavenger when the capacity of IGFBP-3 to bind IGF-1 in the serum is insufficient in patients with prostate cancer. Taken together, these studies strongly support a relationship between IGF-1, specific

IGF-binding proteins and prostate cancer risk. To date, no published studies have examined racial difference in IGF-1 levels or systematically examined these associations in a healthy high risk screening population.

Prostate Specific Antigen (PSA), produced by the prostate epithelium, is elevated in patients with prostate cancer. Thus, PSA is considered a sensitive marker to monitor and detect disease. Studies show that PSA correlates with IGF-binding proteins. Ho et al. (18) found a positive correlation between serum levels of IGFBP-2 and PSA levels in patients with prostate cancer. The study results suggest that serum IGFBP-2 levels, like PSA, may reflect the tumor load in prostate cancer. Kanety et al. (16) also found that serum IGFBP-2 levels and its percentage of the total IGFBPs were highly positively correlated with serum PSA. In that study, a negative correlation was also found between IGFBP-3 and PSA. (16). These studies are consistent with findings in another study that showed IGFBP-2 elevated to a similar mean level when serum PSA was greater than 150 ug/l (17). It was suggested that the proteolysis effect of PSA on IGFBP potentiates the growth-promoting effects of IGF-1 on prostate cells. The researchers believe that PSA might serve to modulate IGF function within the reproductive system or in prostate cancer by altering IGF-IGFBP-3 interaction (17).

Researchers have examined various androgens as possible risk factors for prostate cancer. Ross et al (19) demonstrated that young African-American men had serum testosterone levels that were approximately 15% higher than their white counterparts. Research conducted by Erfurth et al. (20) showed that in a group of healthy men serum levels of IGF-1 increased with increasing free testosterone (p=0.005). In this study IGFBP-1 was significantly and positively correlated with free-testosterone and total testosterone.

Environmental factors, such as obesity and diet, have been shown to influence prostate cancer risk. Obesity has been shown to be associated with endocrine changes and is believed to be a risk factor for prostate cancer. Although the relationship between prostate cancer and obesity is somewhat inconsistent, two retrospective studies (21,22) and several prospective studies (23-26) have reported associations with body mass index (BMI) and prostate cancer risk. Andersson et al. (26) conducted a prospective study of 135,000 male construction workers who were followed for an average of 18 years. This study revealed a positive association of weight, height, BMI and lean body mass with risk of prostate cancer. Moreover, these anthropometric measures were more strongly associated with mortality. Obesity is also believed to be associated with IGF-1 levels. In a study of healthy males, free IGF-1 concentrations were higher in obese subjects than in normal controls (27). IGFBP-2 concentrations were also suppressed in the obese subjects. The researchers suggested that overnutrition and chronic hyperinsulinamia in obesity might alter the regulated growth response by insulin stimulation of IGF-1 production and suppression of hepatic IGFBP-1 and IGFBP-2 production, which may inhibit IGF-1 bioactivity.

Nutrition is a key regulator of IGF's and IGF-binding proteins (28) and prostate cancer risk. Specifically, energy restriction is associated with lower concentrations of IGF-1 (28,29) and a reduction in tumor growth, thus favoring cell apoptosis over cell proliferation (15). Isley et al. (30) showed diets deficient in protein and energy intake decreased IGF-1 levels. In this study, changes in serum IGF-1 concentrations correlated significantly with mean daily nitrogen balance. Also, serum levels of IGFBP-2 and

IGFBP-3 are inversely regulated by dietary protein and caloric intake as well as fasting (28). Investigators (31-33) have shown significant positive associations between total energy intake, dietary fat intake and prostrate cancer risk. These associations were more pronounced for cases with aggressive cancers (31,33). Andersson et al. (33) hypothesized that a high-energy, high fat, high-protein diet might influence prostate cancer risk mediated by IGF-1 concentrations. However, the relationships between IGF-1 and specific nutrients are not well understood, and those factors and the mechanisms of action requires further study.

Diet and obesity may play a significant role in understanding the relationships between serum IGF-1, IGFBP-2 and IGFBP-3 concentrations and prostate cancer risk. We believe serum levels of IGF-1, IGFBP-2 and IGFBP-3 may influence the etiology of prostate cancer and can serve as markers for this disease. Also, a low-fat, high-fiber diet has been shown to decrease circulating testosterone levels by altering male sex hormone metabolism (34,35). The proposed study can increase our understanding of the role of diet and obesity in modulating serum IGF-1 and IGF-binding proteins. Thus, reducing body weight/body fat may prevent or reduce prostate cancer risk. Understanding the associations between IGF-1, specific IGF-binding proteins, testosterone, PSA, BMI and diet in a healthy, screening population may help to better understand the etiology of this disease.

Hypotheses/Purpose

The purpose of this study is to examine racial differences in prostate cancer risk in a healthy high risk screening population of African American and Caucasian males. The associations between IGF-1, IGF-binding proteins (2&3), PSA, testosterone, and BMI will be examined. The study aims to determine racial differences between IGF-1, IGFBP-2, IGFBP-3, PSA, testosterone, BMI, and diets high in calories, protein and fat. Specifically, the study objectives are to:

- define racial differences in serum levels of total IGF-1, IGFBP-2, IGFBP-3, and testosterone
- define how diet and BMI impact serum levels of IGF-1, IGFBP-2, IGFBP-3, testosterone and PSA in African American and Caucasian men.
- determine the associations between serum levels of total IGF-1, IGFBP-2, IGFBP-3, testosterone, PSA, BMI and specific nutrients.

The proposed study will help to explain the increased risk of prostate cancer for African American men and the role of specific nutrients in influencing IGF-1 and IGF-binding protein concentrations.

BODY

Study progress through year three will be described below with respect to each of the tasks in the Statement of Work.

Statement of Work

Task 1: **Hiring and Training of Staff**
The grant was officially awarded December 1999, but did not start until April 2000 due to concerns expressed by the Human Subjects Protection, AMDEX Corporation. In March, a medical research assistant was employed to work on the project. Study protocol was finalized and a training session was held to discuss study goals, objectives, protocols, responsibilities and data collection procedures.

Task 2: **Obtain and review clinical questionnaires of 1,517 men who participated in prostate screenings to identify men eligible for the study**
The clinical questionnaires were obtained from the men who participated in prostate screenings at the Lombardi Cancer Center, Georgetown University. The questionnaires were categorized by race, age, and cancer status. Computer entries of all questionnaires were inputted in Microsoft Excel.

Task 3: **Obtain PSA values for men who are eligible for the study.**
PSA results were obtained for all men and computer entry of results was inputted in Microsoft Excel.

Task 4: **Work with Director of Serum Bank to retrieve serum for men eligible for the study.**
We worked closely with Dr. Bruce Trock, who was the Director of the Serum Bank, Georgetown University to retrieve serum collected from prostate screenings that were stored at the Serum Bank. Dr. Trock informed us that some of the stored samples were frozen in the wrong tubes, stored as whole blood or were not centrifuged. Therefore, we conducted preliminary studies to determine the reliability and validity of IGF-1, IGFBP-2, and IGFBP-3 in whole blood when compared to serum. Samples were obtained from 10 volunteers participating in Dr. Trocks project. Dr. Kevin Cullen, who is an investigator with this project, had his laboratory to conduct the comparative analysis. Results from the analysis revealed that the samples were not appropriate for our study. Therefore, we recruited new men who came to prostate screenings at the Lombardi Cancer Center and the Howard University Cancer Center. A total of 544 men were recruited for this project.

Task 5: **Analyze serum for IGF-1, IGFBP-2, IGFBP-3 and testosterone.**
Serum analysis was conducted in Dr. Kevin Cullen's laboratory at the
Lombardi Cancer Center. A total of 1,923 assays were completed. This
includes the following: 438 assays analyzed for IGF-1; 506 assays
analyzed for IGFBP-2; 444 assays analyzed for IGFBP-3 and 535 assays
were analyzed for testosterone. *See appendices for assay methodology,
assays completed and standard curves.*

Task 6: **Stratify and randomize over 300 men for telephone interview.**
We have stratified 300 men who are eligible for the telephone interview.

Task 7: **Send letters to 300 men requesting telephone interview.**
Letters were sent to 300 men who were stratified requesting an interview.

Task 8: **Call 300 men to schedule telephone interview.**
A total of 300 men were called to schedule a telephone interview.

Task 9: **Conduct telephone interview.**
A total of 138 men, which consisted of 83 African Americans and 55
Caucasians agreed to complete the short nutrition questionnaire over the
phone. There were many reasons for the low participation of men
scheduled to be interviewed. Some reasons included non working
telephone numbers and no answer. However, many of the men we were
able to contact, were not interested or stated they were too busy to
participate.

Task 10: **Mail monetary incentive to interviewees.**
Monetary incentives were mailed to all men who completed the nutrition
questionnaire over the telephone.

Task 11: **Data entry and analyze; complete final report.**
Data entry was completed for 138 nutrition questionnaires and 1,923
serum assays consisting of IGF-1, IGFBP-2, IGFBP-3 and testosterone.
Serum analysis and data entry are complete and a final report of the study
results is enclosed.

KEY RESEARCH ACCOMPLISHMENTS

- Hiring and training of personnel working on project.
- Finalization of study protocol.
- Obtained and reviewed clinical questionnaires of 1,517 men who had stored serum
- Preliminary analysis to determine if stored blood was appropriated for our study.
- Obtained PSA values for men who had stored blood.
- Data entry of clinical information from questionnaires and PSA values.
- Recruited 544 men who participated in recent prostate screening.
- Completed 1,923 IGF-1, IGFBP-2, IGFBP-3 and testosterone assays.
- Stratified, randomized and called 300 men for the telephone interview.
- Conducted telephone interview with 138 study participants.
- Data entry of 138 nutrition questionnaires from telephone interviews.
- Data entry of 1,923 of IGF-1, IGFBP-2, IGFBP-3 and testosterone assays.
- Statistical analysis completed.
- Final report completed.

REPORTABLE OUTCOMES

INITIAL ANALYSIS REPORT

METHODS

The initial task was to synthesize multiple data sets containing (1) serum data results from men attending the Georgetown Medical Center (GUMC) screening, (2) linkage between GUMC serum identification numbers and nutrient data identification numbers, as well as age, height, weight, PSA, marital status, BPH and DRE results (3) nutrient data for GUMC subjects, and (4) serum data for men attending the Howard University Expo (Expo) screening (all were African American). This task was initially complicated by embedded formatting in the EXCEL data files, duplicate values for some patients, data miscoding, and identification of men for whom key data were missing. All data analyses were performed with SAS (SAS Institute, Cary, NC).

The following data were considered in the analyses described herein:

GUMC screenees

Age
Race
Height
Weight
BMI
Marital status
IGF1
IGFBP2
IGFBP3
Testosterone
PSA
Prostate size (g)
DRE result
Caloric intake
Protein
Total fat
Carbohydrates

Expo screenees (Howard University)

IGF1
IGFBP2
IGFBP3
Testosterone

A large number of other dietary/nutrition variables are available for GUMC screenees. These will be evaluated in subsequent analyses.

Analyses were divided into two stages:

Group 1. Analysis of effects of race and nutrients on IGF1 and IGF binding proteins. These analyses included all men with valid data from the GUMC screening program who also had nutrient data available. Analyses focused on comparisons of means between African American and white men. Distributions of serum variables were first evaluated to identify departures from normality, using the Kolmogorov-Smirnov test. Differences in means were tested using the t-test for variables that conformed to a normal distribution (or which conformed to normality after a logarithmic transformation), or the Wilcoxon nonparametric test for variables that were not normally distributed. Analysis of variance (ANOVA) and analysis of covariance (ANCOVA) were used to allow means to be

compared between the two race groups, while adjusting for other potential confounders. Univariate and multiple linear regression analyses were also used to evaluate linear correlations among IGF variables and nutrients, and ANCOVA was used to compare IGF variables between African American and white men, while adjusting for other factors.

Group 2. Analysis of race differences in serum IGF1 and IGF binding proteins. This analysis included all men with valid data from the GUMC and Expo screening programs. Analyses primarily focused on comparison of mean values between African American and white men, as described in the previous section.

RESULTS

Descriptive Data

There were 198 African American men and 111 white men among the GUMC screenees. There were 150 African American men and no white men among the Expo screenees. Demographic and clinical data are available only for the GUMC men; these are described below only for the GUMC men for whom nutrition data were also available, i.e. Group 1.

Table 1 shows that African American men were significantly younger than white men, and had somewhat higher BMI, although this difference was not statistically significant. Other factors were similar in both ethnic groups, with the majority of men being married, and most have a normal prostate exam.

Race differences in IGF1, IGF binding proteins and nutrients: GUMC screenees

Table 2 shows that African American men had significantly lower levels of IGFBP2, and significantly higher levels of testosterone, but were not significantly different from white men with respect to IGF1, IGFBP3, PSA. Adjustment for age, or age and BMI using ANCOVA did not alter these associations.

Table 3 shows the results of multiple linear regressions to examine the effects of age on IGF1, IGF binding proteins, testosterone and PSA, while controlling for BMI, separately among African American and white men. Statistically significant p-values are indicated in bold font for ease of interpretation. Among African American men, PSA was the only measure significantly associated with age, while among white men, the logarithm of IGFBP2 (ln[IGFBP2]) was significantly associated with age and BMI, while PSA exhibited a nearly significant association with age. Despite the non-significant p-value (p=0.129) for the association of age with ln[IGFBP2] among African American men, the estimated regression slope (0.012) was very similar to the slope among white men (0.015); the latter was statistically significant. This suggests that IGFBP2 may increase with age among both races at a similar rate. In these models, BMI was negatively associated with IGFBP2 for both races; both associations were statistically significant.

Table 4 compares nutrient values by race. African American men had higher intakes than white men of calories, protein, fat and carbohydrates; all but the latter were statistically significant.

Linear regressions were performed to evaluate the association of IGF1, IGF binding proteins and testosterone (dependent variables) on the above nutrients (dependent variables), adjusted for age and BMI. These analyses were performed separately by race, then for both races combined. In these analyses the primary interest was on the slope of the regression parameter for the nutrient, i.e. the direction and statistical significance of the relationship between the IGF-measure and the nutrient. Again, p-values that are statistically significant are shown in bold font. The only serum measure that exhibited any indication of a trend with nutrient values was the logarithm of IGFBP2 (ln[IGFBP2]). Even though the parameter estimates for the regressions of ln[IGFBP2] on the nutrients were rarely statistically significant, they are presented in Table 5 because the trends are still suggestive, particularly for both races combined.

Table 5 shows that all four nutrients (calories, protein, total fat and carbohydrates) were always negatively associated with IGFBP2. The associations were not statistically significant, although among whites the association with calories approached significance (p=0.088). For both races combined the association with calories attained statistical significance, p=0.043, and that with total fat approached significance (p=0.085). The association between IGFBP2 and age, and the negative association with BMI are very constant for each race.

Because of the relatively small sample size, it is possible that inclusion of both age and BMI may reduce statistical power. Univariate regressions of age of the nutrients on age and BMI indicated that neither age nor BMI were significant predictors of nutrient level. Therefore, it is unlikely that they confound the association between IGFBP2 and nutrients, and may be reducing the efficiency of the models. Accordingly, the regression analyses were repeated as univariate regressions of ln[IGFBP2] on the nutrients alone, for both races combined. These results are presented in Table 6. In these analyses, IGFBP2 exhibits a significant negative association with calories, protein and total fat.

Linear regressions were also performed to evaluate associations between IGF-measures and PSA, represented by ln[PSA] because PSA did not exhibit a normal distribution. Only IGFBP3 exhibited a significant inverse association with ln[PSA], and only among whites, with slope = - 496.8, p=0.026. No other IGF measures were significantly correlated with PSA, either positively or negatively.

Race differences in IGF1 and IGF binding proteins: GUMC and Expo screenees

Table 7 shows comparisons of mean levels between African American and white men in this large combined screening population. Serum IGFBP2 was significantly lower among

African American men, while IGFBP3 and testosterone were significantly higher. There were no significant differences in IGF1.

ANCOVA was used to compare IGF1 by race, adjusting for either IGFBP2 or IGFBP3. Neither association with race was statistically significant (p=0.278 and 0.954, respectively).

SUMMARY

These analyses show that IGFBP2 is significantly lower in African American than white men, while IGFBP3 and testosterone are significantly higher. IGFBP2 also exhibits a significant inverse association with BMI for both races, and a positive association with age for whites. African American men have higher consumption of calories, protein, total fat and nutrients than whites; all but the latter difference are significant. Finally, IGFBP2 exhibits a significant univariate negative correlation with calories, protein and total fat, with a somewhat stronger association among white than African American men. Adjustment for age and BMI made all but the association with calories no longer significant, but it is possible that this represents over-adjustment of the model since age is not significantly correlated with nutrient intake in these men.

Table 1. Demographic and clinical data for GUMC screenees who provided dietary data.

variable	African American (n=77)	White (n=51)	test of means*
age	54.4	61.2	< 0.0001
height (in.)	69.9	69.8	0.881
weight (lbs.)	193.6	183.1	0.117
BMI	28.0	26.4	0.069
Marital status (%)			0.809
Married	53.3	52.9	
single	27.3	21.6	
divorced	14.3	15.7	
widowed	1.3	3.9	
unknown	3.9	5.9	
Prostate size (g)			0.685
15-20	13.3	10.2	
21-30	12.0	16.3	
31-40	9.3	10.2	
41 +	0.0	2.0	
unknown	65.3	61.2	
DRE result			0.139
normal	84.2	81.6	
abnormal/ not suspicious	5.3	0.0	
BPH	10.5	18.4	

* p-value from t-test, except for BMI where p-value is from Wilcoxon test

Table 2. Comparison of IGF1, IGF binding proteins, testosterone, and PSA among African American and white men from GUMC screening who also provided nutrient data.

variable	African American (n=77)	White (n=51)	test of means*
IGF1	138.3	143.4	0.556
IGFBP2	409.1	546.3	0.011
IGFBP3	3426.4	3472.4	0.770
Testosterone	4.48	3.88	0.030
PSA	1.29	1.40	0.525

* p-value from t-test, except for IGFBP2, testosterone and PSA, where p-values are from Wilcoxon test

Table 3. Multiple linear regression of IGF1, IGF binding proteins, testosterone and PSA on age, controlling for BMI: Analyses by race, among men from GUMC screening who also provided nutrient data.

a. African American men:

| variable | intercept | Regression parameters (p-values) | | overall model |
		age	BMI	p-value
IGF1	188.2	- 0.86 (0.143)	- 0.16 (0.850)	0.320
ln(IGFBP2)	6.14	0.012 (0.129)	- 0.033 **(0.005)**	**0.001**
IGFBP3	3571.9	-12.48 (0.285)	18.46 (.292)	0.360
ln(testos.)	1.94	- 0.003 (0.719)	- 0.015 (0.198)	0.385
PSA	- 1.52	0.026 **(.005)**	0.003 (0.831)	**0.018**

b. White men:

| variable | intercept | Regression parameters (p-values) | | overall model |
		age	BMI	p-value
IGF1	170.9	- 0.74 (0.276)	0.67 (0.691)	0.498
ln(IGFBP2)	6.74	0.015 **(0.042)**	- 0.058 **(0.002)**	**0.001**
IGFBP3	3734.4	7.00 (0.568)	- 26.13 (.407)	0.596
ln(testos.)	1.08	0.008 (0.413)	- 0.016 (0.503)	0.566
PSA	- 0.77	0.015 (.067)	0.001 (0.942)	0.184

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Table 4. Comparison of nutrients among African American and white men from GUMC screening who also provided nutrient data.

variable	African American (n=77)	White (n=51)	test of means
calories	1862.5	1596.5	0.017
protein	75.8	64.8	0.029
total fat	74.6	58.1	0.006
carbohydrate	210.9	189.5	0.082

Table 5. Multiple linear regression of ln(IGFBP2) on nutrients, adjusted for age, BMI: Analyses by race, among men from GUMC screening who also provided nutrient data.

a. African American men

nutrient	intercept	regression parameters (p-values)			overall model
		nutrient	age	BMI	
calories	6.41	- 0.0001 (0.225)	0.011 (0.161)	- 0.034 (**0.004**)	**0.013**
protein	6.33	- 0.002 (0.360)	0.011 (0.168)	- 0.033 (**0.005**)	**0.018**
total fat	6.28	- 0.002 (0.374)	0.011 (0.145)	- 0.033 (**0.005**)	**0.018**
carbohydrate	6.35	- 0.0008 (0.345)	0.012 (0.130)	-0.034 (**0.009**)	**0.018**

b. White men

nutrient	intercept	regression parameters (p-values)			overall model
		nutrient	age	BMI	
calories	7.11	- 0.0003 (0.088)	0.015 (**0.039**)	- 0.055 (**0.003**)	**0.001**
protein	7.04	- 0.006 (0.115)	0.015 (**0.043**)	- 0.053 (**0.004**)	**0.001**
total fat	6.96	- 0.004 (0.121)	0.014 (**0.049**)	- 0.055 (**0.003**)	**0.001**
carbohydrate	7.03	- 0.002 (0.265)	0.015 (**0.048**)	-0.056 (**0.003**)	**0.003**

c. Both races combined

nutrient	intercept	regression parameters (p-values)			overall model
		nutrient	age	BMI	
calories	6.51	- 0.0001 (**0.043**)	0.014 (**0.004**)	- 0.041 (**<0.0001**)	**<0.0001**
protein	6.42	- 0.003 (0.106)	0.014 (**0.005**)	- 0.040 (**<0.0001**)	**<0.0001**
total fat	6.38	- 0.002 (0.085)	0.015 (**0.004**)	- 0.040 (**<0.0001**)	**<0.0001**
carbohydrate	6.45	- 0.001 (0.119)	0.015 (**0.003**)	-0.041 (**<0.0001**)	**<0.0001**

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Table 6. Linear regression of ln(IGFBP2) on nutrients: Both races combined, among men from GUMC screening who also provided nutrient data.

nutrient	intercept	regression parameter	p-value
calories	6.261	- 0.0002	**0.026**
protein	6.22	- 0.004	**0.033**
total fat	6.17	- 0.003	**0.033**
carbohydrate	6.19	- 0.001	0.129

Table 7. Comparison of IGF1, IGF binding proteins, and testosterone among African American and white men in the combined GUMC and Expo screening populations.

variable	African American (n=348)	White (n=111)	test of means*
IGF1	141.8	140.2	0.758
IGFBP2	410.0	517.6	0.002
IGFBP3	3770.8	3493.6	0.012
Testosterone	4.06	3.76	0.011

* p-value from t-test, except for IGFBP2 and testosterone, where p-values are from Wilcoxon test

CONCLUSIONS

Study personnel was hired and trained. The clinical protocol was finalized.
Approximately 1500 clinical questionnaires were reviewed to determine study eligibility.
Data entry of clinical information and PSA's were completed for all eligible subjects.
However, there were unanticipated obstacles in sorting out which frozen blood samples
were appropriate for analysis of study variables. Preliminary analysis was conducted to
compare the validity ad reliability of IGF-1, IGFBP-2, and IGFBP-3 in whole blood
versus serum. It was determined that the frozen blood samples (whole blood was not
appropriate for use in this study.

Since the frozen samples of whole blood could not be used for this project, we began
recruiting men who attended prostate screening at the Lombardi Cancer Center and the
Howard University Cancer Center. The study recruited 544 men. From these men,
1,923 assays were analyzed for IGF-1, IGFBP-2, IGFBP-3 and testosterone. A total of
300 men were stratified and randomized for the telephone interview. Letters requesting a
telephone interview were sent to 300 men. Of this number 138 were interviewed to
determine nutrition intake.

In March 2003, we requested a no-cost one-year extension for this project to allow
additional time to complete serum analysis, data entry, data analysis and final report. Our
request was approved on March 21, 2003.

Final Report

The purpose of this study is to examine racial differences in prostate cancer risk in a
healthy high risk screening population of African American and Caucasian males. The
associations between IGF-1, IGF-binding proteins (2&3), PSA, testosterone, and BMI
were examined. Over five hundred African American and Caucasian men were recruited
for this study. A subset of this group were administered a food frequency questionnaire
over the telephone. The analysis report examining study hypothesis was completed and
findings are below.

Primary hypotheses
1. African American men will have elevated levels of total IGF-1, IGFBP-2,
   testosterone and decreased levels of IGFBP-3 than aged matched men.

   Findings: We did not find elevated levels of total IGF-1 in African American
   men. Surprisingly, we found that IGFBP-3 was higher in African American
   men and IGFBP-2 was significantly higher in Caucasian males (p=0.011).
   African American men did have statistically significant elevated levels of
   testosterone (p=0.030) when compared to Caucasians males.

2. Serum levels of IGF-1 and IGFBP-2 in African American men are associated
   with a diet high in calories, protein, and fat.

Finding: Serum levels of IGF-1was not associated with a diet high in calories, protein, and fat in African American men. IGFBP-2 exhibited a significant <u>univariate</u> negative correlation with calories (p=0.026), protein (p=0.033) and total fat (p=0.033), with a somewhat stronger association among white than African American men.

Overall, the analyses show that IGFBP2 is significantly lower in African American than white men, while IGFBP3 and testosterone are significantly higher. IGFBP2 also exhibits a significant inverse association with BMI for both races, and a positive association with age for whites. African American men have higher consumption of calories, protein, total fat and nutrients than whites; all but the latter difference are significant. Finally, IGFBP2 exhibits a significant <u>univariate</u> negative correlation with calories, protein and total fat, with a somewhat stronger association among white than African American men. Adjustment for age and BMI made all but the association with calories no longer significant, but it is possible that this represents over-adjustment of the model since age is not significantly correlated with nutrient intake in these men.

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APPENDICES

LIST OF ABBREVIATIONS AND ACRONYMS

IGF	insulin growth factor type 1
IGFBP-2	insulin growth factor binding protein 2
IGFBP-3	insulin growth factor binding protein 3
PSA	prostate-specific androgen

Meeting abstracts during reporting period: None in connection with this project

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